THE INFLUENCE OF THE THYROID GLAND AND OF THE OVARY ON THE METABOLISM OF IODINE

AN EXPERIMENTAL STUDY IN THE DOG

H. J. PERKIN AND BROCK R. BROWN[1]
From the Research Foundation of The Lahey Clinic
BOSTON, MASSACHUSETTS

In the course of a series of investigations concerning the level of iodine in the blood of dogs receiving Lugol's solution, certain experimental data were considered to indicate the existence of a correlation between the thyroid gland, the metabolism of iodine and the ovary. The experimental observations are detailed in the present report.

METHODS AND RESULTS

For the purpose of presentation, the experiments cited have been divided into 4 groups. *A.* The *influence of the daily ingestion of a specific amount of iodine on the blood iodine level of normal dogs.* Six female and 4 male dogs of the same breed and proportionate body weights (40 to 50 lb.) were given daily doses of Lugol's solution for periods ranging from 1 to 12 months. Lugol's solution, equivalent to 72 mg. of iodine, was administered by stomach tube daily at the same time. Prior to the giving of the iodine, 1 cc. of blood was withdrawn from the femoral vein for iodine analysis (1, 2). The animals received one meal a day, consisting exclusively of meat, immediately after the blood had been collected.

The results (fig. 1 and 2) showed that the blood iodine level of normal male and female dogs receiving daily 72 mg. of iodine represented graphically a series of peaks and dips varying from 750 to 2500 γ of iodine per 100 cc. of whole blood. The rise and fall of the level of iodine in the blood appeared to be more regular in female (fig. 1) than in male dogs (fig. 2). In one female dog which received iodine for a year, a very high peak of elevation in blood iodine occurred in the spring and again during the autumn. This peak may be attributed to seasonal influence, the period of fertility, or unknown factors (fig. 1).

Coincidental to the above, a normal animal became pregnant. The pregnancy followed a natural course with the animal continued on experiment. In this animal, the blood iodine level was appreciably depressed throughout the period of gestation (fig. 3). After the delivery of two normal pups, the blood iodine level rose, and maintained the same graphical relationship as previous to the pregnancy (fig. 3).

B. The influence of total extirpation of the thyroid gland on the blood

[1] Formerly of the Department of Medical Research, University of Toronto, Toronto, Canada.

iodine level of male and of female dogs ingesting the same specific amount of iodine daily. Four female and two male dogs from group *A* were subjected to complete thyroidectomy. Although the parathyroid glands were transplanted, the animals showed signs of hypoparathyroidism up to two weeks following operation. The attacks of tetany were treated by giving parathormone, together with calcium chloride and viosterol in milk. After 3 or 4 episodes were relieved, no further treatment was necessary. On complete recovery

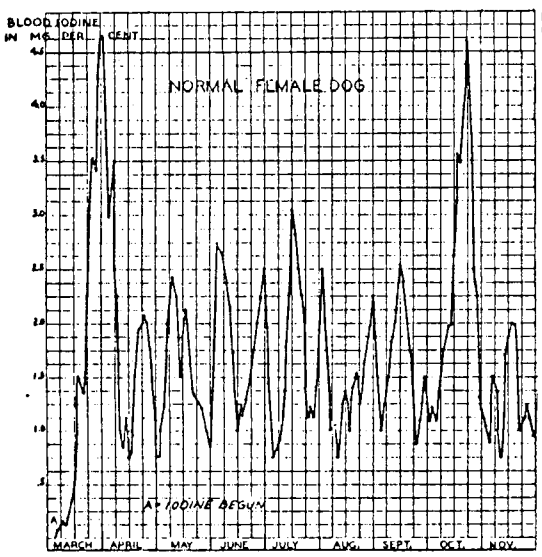

Fig. 1.

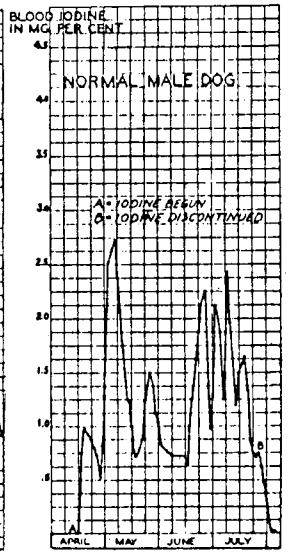

Fig. 2.

from the operation, the dogs were again given the same dose of iodine (72 mg.) daily, and their blood iodine levels were followed.

The results in female dogs revealed that the variations in the blood iodine level were unaffected by the removal of the thyroid gland (compare fig. 1 and 4). In contrast, the blood iodine level of male dogs showed a considerable decrease from that found prior to thyroidectomy (compare fig. 2 and 5), or in thyroidectomized female dogs (compare fig. 4 and 5). The comparative relationship as shown in figures 4 and 5 is believed to indicate the existence of a variation attributable to the sex of the animal.

C. The influence of extirpation of the ovary on the blood iodine level of thyroidectomized female dogs receiving 72 mg. of iodine daily. Bilateral oophorectomy was performed on two of the thyroidectomized female dogs. Following this procedure, iodine was again administered in the same daily dosage and the blood iodine levels were followed.

The results indicated that, following removal of the ovaries from thyroidectomized dogs, the blood iodine level fell in comparison with the previous level in the same thyroidectomized animal (compare fig. 4 and 6). The blood iodine graph of the female dogs on which oophorectomy and thyroidectomy

had been performed simulated that of the thyroidectomized male dogs (compare fig. 5 and 6). These findings indicated that the difference in the blood iodine level between male and female thyroidectomized dogs, noted in group *B*, was eliminated by the removal of the ovaries of the latter.

D. Iodine analysis of the tissues of dogs which had received iodine for varying lengths of time. At the conclusion of the above experiments, autopsy was performed on all of the animals, and iodine analyses were carried out on

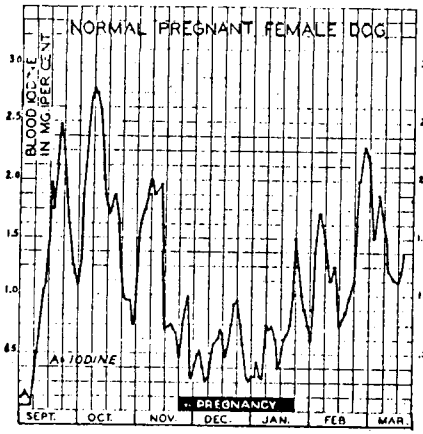

Fig. 3.

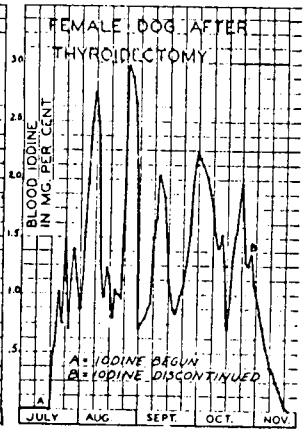

Fig. 4.

the various tissues. The values cited in table 1 were representative of the entire group.

From the table, it will be seen that the ovary contained approximately twice as much iodine as any other tissue, except the thyroid gland. Furthermore, the iodine content of the thyroid gland apparently increased with the period of time that iodine was administered.

DISCUSSION

In the present study, the more important factors affecting the level of iodine in the blood at any given time were considered to be *a)*, the amount of iodine administered, *b)*, the rate and extent of absorption, *c)*, the excretion and endogenous processes. In the first instance, it should be noted that the iodine administered daily was an excessively large amount to be given in a single dose. If divided doses had been given, a more cumulative effect than that obtained might have resulted. In view of the repeated doses and the large amount, the form of iodine used in these experiments was probably not important. Regarding absorption, it would seem logical to assume that the iodine administered was taken up quickly and completely into the blood, since unpublished data (3) showed that, following the administration of a single dose of iodine, the blood evidenced absorption within 5 minutes, with the feces devoid of a significant quantity of iodine until the third day. The complete absorption of the inorganic iodides of sodium and of potassium from the gastro-intestinal tract has also been noted by Greenbaum and Raiziss (4).

Under the present experimental conditions, it seemed reasonable to believe that the animal body would have become saturated with iodine, the excess being excreted. Since signs of iodism were not apparent in the animals, and analysis of the tissues revealed no marked accumulation of iodine, an equilibrium between absorption and excretion must have been established. Furthermore, the effect of absorption and excretion was minimized by taking blood for iodine analysis during the postabsorptive state. With these ideas in mind, the predominant influence on the blood iodine level appeared to be attributable to endogenous factors.

That the blood iodine level of normal dogs receiving 72 mg. of iodine daily fluctuated within a definite range seemed remarkable. This variation of rise and fall in the level was not due to experimental error, because an adequate number of iodine analyses indicated the trend of each variation in the level.

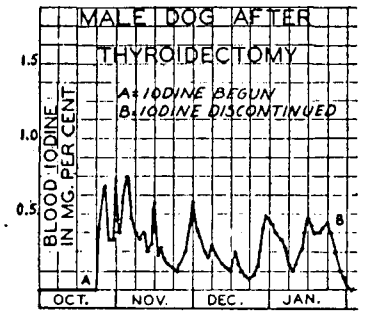

Fig. 5.

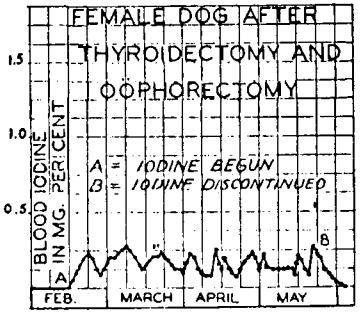

Fig. 6.

The results showed neither an accumulative effect nor a decreased tolerance to iodine. The fluctuations in blood iodine could be explained on the basis that the postabsorptive blood iodine level is dependent on the organic-inorganic iodine ratio in the blood. Such an explanation would necessarily assume that the thyroid gland, with its capacity to combine iodine in an organic form, would be the primary tissue affecting the control of the blood iodine level. The foregoing interpretation was not entirely supported by experimental data, since we have found that alcohol-insoluble fractions of the blood in the above instances gave iodine values of only one-sixth to one-twelfth of the total iodine content. However, the 'organic iodine fraction' did vary in quantitative relationship to the total blood iodine. With such an excess of alcohol-soluble iodine in the blood, it would appear that in these experiments tissues other than the thyroid gland must have exerted an effect on the blood iodine level. That tissues outside the thyroid gland affecting the metabolism of iodine may have been directly or indirectly influenced by the thyroid gland cannot be denied.

The comparative reduction of the blood iodine level in male dogs following thyroidectomy indicated that the thyroid gland is a primary factor in controlling the blood iodine. As pointed out above, the exact nature of this control is not clear. The presence of controlling factors outside the thyroid gland

was apparent because, under the conditions of the experiment, thyroidectomy in female dogs did not appreciably alter the blood iodine level. Since a comparative decrease was found in the blood iodine level, following oophorectomy in thyroidectomized female dogs, it follows that the ovary must have exerted an influence on the blood iodine level. In addition, the present findings indicated that the blood iodine level is influenced to the same degree by the ovary as by the thyroid gland, although this was not confirmed by removing the ovaries and leaving the thyroid gland intact. In this connection, the discovery

TABLE 1. THE IODINE CONTENT OF THE TISSUES OF DOGS RECEIVING IODINE DAILY.

	Mg. of iodine per cent (wet tissue)			
	A[1]	*B*[2]	*C*[3]	*D*[4]
Thyroid	18.3	27.6	31.2	34.6
Kidney	0.21	0.31	0.35	0.43
Liver	0.16	0.42	0.38	0.33
Lung	0.21	0.34	0.29	0.37
Heart muscle	0.24	0.33	0.32	0.30
Adrenal	0.19	0.52	0.41	0.29
Ovary	0.43	0.66		0.63
Testis			0.36	
Bile	0.20	0.28	0.27	0.26
Blood	0.24	0.36	0.42	0.46
Feces	0.20			
Intestine	0.18			

[1] *Animal A* received iodine daily for 1 month.
[2] *Animal B* received iodine daily for 4 months.
[3] *Animal C* received iodine daily for 7 months.
[4] *Animal D* received iodine daily for 12 months.

of a proportionately high content of iodine in the ovarian tissue served as further evidence favoring an iodine-ovarian relationship, thus confirming the observations of Zoeppritz (5) and Weinberg (6).

SUMMARY

The blood iodine level of male and female dogs receiving 72 mg. of iodine daily was represented graphically as a series of peaks and dips varying from 75 to 2500 γ of iodine per cent of whole blood. The blood iodine level was considerably depressed following complete thyroidectomy in male dogs receiving iodine. In female dogs receiving iodine, complete thyroidectomy apparently had no influence on the blood iodine level. Following bilateral oophorectomy in the thyroidectomized female dogs, the blood iodine level decreased; the results simulated the values found in thyroidectomized male dogs.

Iodine analyses of the tissues of dogs receiving iodine for varying periods of time indicated that, exclusive of the thyroid gland, the ovary contained approximately twice the amount of iodine per gram weight of any other tissue.

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